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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/899,303	07/06/2001	Geert Maertens	BJS-2551-109	3515

23117 7590 04/18/2007
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EXAMINER	
LI, BAO Q	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/899,303	MAERTENS ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69,70,73,74,76,87-90,95-97 and 102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69,70,73,74,76,87-90 and 102* is/are rejected.

7)☒ Claim(s) *95-97* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This is a response to the amendment filed on 02/22/07. Claim 76 has been amended. Claims 1-68, 71-72, 75, 77-86, 91-94 and 98-101 have been canceled. Claims 69-70, 73, 76, 87-90, 95-97 and 102 are pending before the examiner.

Priority

The priority document EP 94870132.1, filed on July 29, 1994 has been acknowledged and reviewed.

Claim Rejections - 35 USC § 102

Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action

The jection of claims 76 and 87 under 35 U.S.C. 102(b) as being anticipated by Hsu et al. (Hepatology, May 1993, Vol. 17, No. 5, pp. 763-771) has been withdrawn necessitated by applicants' amendment.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 69-70, 73, 74, 76, 87-90 and 102 are still rejected under 35 U.S.C. 103(a) on the same ground stated in the previous office action, as being unpatentable over Hsu et al. (Hepatology, May 1993, Vol. 17, No. 5, pp. 763-771) in view of the disclosures by Ralston et al. (WO 92/08734A1), Tartaglia et al. (Virol. 1992, Vol. 188 (1), pp. 217-232), Sutter et al.(Proc. Natl. Acad. Sci. USA. 1992, Vol. 89, pp. 10847-10851) and Vanderbroeck et al. (Eur. J. Biochem. 1993, Vol. 217, pp. 45-52).

3. Applicants' traverse the rejection and submit the following arguments:

4. 1). Hsu teaches expression of an E1 construct in a baculovirus, but he fails to teach or suggest or motivate one or ordinary skill in the art to use vaccinia vectors for HCV E1 expression;

5. 2). While Ralston et al. teach to use vaccinia viral vector to express the HCV E1, they do not teach HCV E1 construct having same boundaries since the HCV envelope protein E1 or E2 has hydrophobic domain deletion in 170-190, aa 260-290, or aa 330-380 of E1, and E2 has a deletion at aa 660-830.

6. 3). The references by Tartaglia et al. and Sutter et al. only teach using NYVAC or MVA as expression viral vector, they do not teach to express the HCV E1 protein with defied boundaries cited in claim 69 or claim 70.

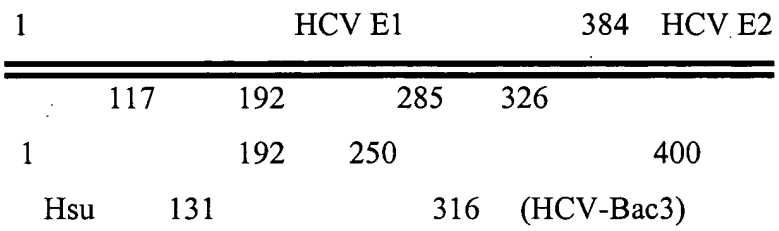
7. 4). Regarding the reference by Vanderbroeck et al. Applicants argue that the cited reference is only related to claim 74. However; Applicants further require an explanation of the relevance of the reference to the pending claims.

8. Finally, applicants conclude that Hsu teaches away from the claimed invention. Tartaglia and Sutter do not add anything to Ralston with regard to the subject matter of the pending claims. Vanderbreock is not believed to cure the deficiencies of the combination of Hsu, Ralston, Tartagia and Sutter. Applicants therefore, assert that all references in combination would not have lead one of ordinary skill in the art to have made the presently claimed invention.

9. Applicants' arguments have been respectfully considered; however, it is not found persuasive. First, applicant's arguments is against the references individually. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

10. In the instant case, the reference by Hsu et al. teaches a method of using a recombinant viral vector to express a HCV E1 protein, wherein the HCV E1 antigen ranges from amino acid 133 to 316 (HCV-Bac 3), which meets the limitation as claims 69 and 76 broadly drafted since the claimed HCV E1 starts in the region between amino acid positions 117-192 and ends in the region between amino acid positions 285-326 (claim 69) or starts in the region between amino acid positions 1-192 and ends in the region between amino acid positions 250-400 (claim 76).

The 133 is located in between 1-192 or 117-192 and 326 is located in between 285-326 or between 250-400.



11. Applicants also argue that claim 70, which is dependent on claim 69, requires that the 1st hydrophobic domain of E1 should be present (170-190), the HCV E1 fragment taught by Hsu et al. ranges from 133 to 316 inherently contains the portion from 170-190. Therefore, the reference by Hsu'e does not teach away from the claimed invention.

12. While Hsu et al. do not teach to use vaccinia viral vector, particularly using avipox viral vector or Ankara modified virus to expressing the HCV E1 with histidine tag and Xa cleavage site, the vaccinia viral vector is a very common viral vector used for expressing a recombinant viral antigen or any recombinant protein as evidenced by Ralston et al. or Tartaglia et al. or Sutter et al. Therefore, a vaccinia vector preferably, a avipox virus vector cited in claim 89 or Ankara modified virus (AMV) vector cited in claim 90, are all clearly taught by other cited references.

13. Ralston et al. teach to use vaccinia viral vector for efficiently expressing HCV E1. More importantly, Ralston et al. does not teach that the vaccinia vector is only suitable for expressing the HCVE1 with hydrophobic domain deletion(s). In the contrary to applicants' argument that Ralston's reference does not teach to express the HCV E1 protein with exactly same size, since the reference by Hsu et al. already teach the HVC E1 that meets the limitations as claims 69 and 76were drafted. Moreover, Ralston states that experiments should be done to determine which regions should be deleted for optimum results (p. 11). It is obvious to optimize a variable which is expected to affect the outcome of a process, particularly when the prior art explicitly suggests such optimization.

14. The reference by Tartaglia et al. as applicants had already admitted in the response, teaches that the avipox virus canarypox (ALVAC) as a highly attenuated avian vaccinia virus. The more explanation about why a avipox virus is bused as a vector is that said viral vector has many advantages as an expression vector cited in the previous office action (See paragraph 9): (a) no detectable duration or ulceration at the site of inoculation on rabbit skin; (b) rapid clearance of infection from the intradermal inoculation site on rabbit skin; (c) absence of any testicular inflammation in nude mice; (d) greatly reduced virulence as demonstrated by the results of intracranial challenge of both 3-week-old or newborn mice; (e) greatly reduced pathogenicity and failure to disseminate in immunodeficient (nude or cyclophosphamide treated) mice; (f) dramatically reduced ability to replicate on a variety of human tissue culture cells. and (g). the vector made by NYVAC strain retains the ability to induce strong immune responses to extrinsic antigens.

15. The reference by Sutter et al. also admitted by applicants, teaches that the modified vaccinia Ankara (MVA) as a highly attenuated vaccinia virus has been safety tested in human and approved to be a valuable efficient expression vector for expressing any heterologous gene.

16. Regarding the fusion tag of Histidine or a factor-Xa cleavage site, Vanderbroeck et al. explicitly teach a method about how to use a factor-Xa cleavage site and histidine tag together for expressing a fusion protein. More importantly, Vanderbroeck et al. teach that a fusion protein containing both or one of the tags can be more easily identified and efficiently purified with a commercial chronographic procedure. Vanderbroeck et al. also disclose to use 6 histidine codons as fusion tag in the construct (See Abstract and Materials and Methods disclosed on pages 45-47).

17. Regarding the argument that there is not teaching or suggestion or motivation for the combination of all cited references, MPEP cites: to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.

18. In the instant case, the motivation to modify or to combine the references is the knowledge of an ordinary skill in the art for using vaccinia viral vector including the particular vaccinia viral vector, ALVAC or MVA to express a recombinant protein including a HCV E1

recombinant protein because such knowledge as disclosed by the cited references had been generally available for an artisan with an ordinary skill in the art prior to the current application originally filed.

19. Since the cited references teach all limitations of the claims, and the general knowledge for using a vaccinia viral vector to express a recombinant HCV envelope protein had been available for an person with an ordinary skill in the art prior to the current application originally filed, absence unexpected result, the claimed method is still considered as a prima facie case of obviousness. The rejection is maintained.

Conclusion

Claim 95-97 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claims are allowed.

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bao Qun Li
April 10, 2007

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